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PATENT & TRADEMARK OFFICE

#8

PATENT  
ATTORNEY DOCKET NO. 00742/060002

Certificate of Mailing: Date of Deposit: October 4, 2001

I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Mary Janie DiPalma

Printed name of person mailing correspondence

*Mary Janie DiPalma*

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: R. John Collier et al.

Art Unit: 1646

Serial No.: 09/848,909

Examiner:

Filed: May 4, 2001

Customer No.: 21559

Title: COMPOUNDS AND METHODS FOR THE TREATMENT AND  
PREVENTION OF BACTERIAL INFECTION

Assistant Commissioner For Patents  
Washington, DC 20231

INFORMATION DISCLOSURE STATEMENT

Applicant submits the references listed on the attached form PTO-1449, copies of which are enclosed.

Submission of this statement is not a representation that a search has been made, nor is information included in this statement an admission that the information is material to patentability.

This statement is being filed before the receipt of a first Office action on the merits.

Please apply any charges or credits to Deposit Account 03-2095.

Respectfully submitted,

Date: October 3, 2001

*Kristina Bicker-Brady*

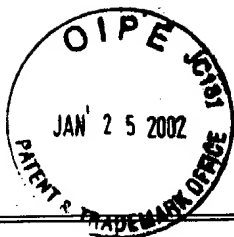
Kristina Bicker-Brady, Ph.D.  
Reg. No. 39,109

Clark & Elbing LLP  
176 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



21559

PATENT & TRADEMARK OFFICE



IDS/#10  
J 1/24/02

PATENT  
ATTORNEY DOCKET NO. 00742/060002

Certificate of Mailing: Date of Deposit: January 11, 2002

I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Mary Jane DiPalma

Printed name of person mailing correspondence

Signature of person mailing correspondence

*Mary Jane DiPalma*

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: R. John Collier et al. Art Unit: 1646  
Serial No.: 09/848,909 Examiner:  
Filed: May 4, 2001 Customer No.: 21559  
Title: COMPOUNDS AND METHODS FOR THE TREATMENT AND  
PREVENTION OF BACTERIAL INFECTION

Assistant Commissioner For Patents  
Washington, DC 20231

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Applicant submits the references listed on the attached form PTO-1449, copies of which are enclosed. A copy of a communication from a foreign patent office in a counterpart application is also enclosed.

Submission of this statement is not a representation that a search has been made, nor is information included in this statement an admission that the information is material to patentability.

This statement is being filed before the receipt of a first Office action on the merits. Please apply any charges or credits to Deposit Account 03-2095.

Respectfully submitted,

Date:

*January 11, 2002*

*Kristina Bieker-Brady*

Kristina Bieker-Brady, Ph.D.  
Reg. No. 39,109

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176 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



21559

PATENT TRADEMARK OFFICE

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: KRISTINA BIECKER-BRADY CLARK & ELBING LLP 176 FEDERAL STREET BOSTON MA 02110-2214
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## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 00742/060W02
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Date of Mailing (day/month/year)	<b>02 JAN 2002</b>
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International application No. PCT/US01/14372
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International filing date (day/month/year)	04 MAY 2001
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Applicant PRESIDENT AND FELLOWS OF HARVARD COLLEGE
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ACTION DUE IDS  
 DUE DATE 7-2-02  
 ESP

1.	<input checked="" type="checkbox"/>	The applicant is hereby notified that the international search report has been established and is transmitted herewith. <b>Filing of amendments and statement under Article 19:</b> The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46): <p style="margin-left: 20px;"> <b>When?</b> The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.                 </p> <p style="margin-left: 20px;"> <b>Where?</b> Directly to the International Bureau of WIPO                      34, chemin des Colombettes                      1211 Geneva 20, Switzerland                      Facsimile No.: (41-22) 740.14.35                 </p> <p style="margin-left: 20px;">For more detailed instructions, see the notes on the accompanying sheet.</p>	INITIALS <u>J.M.</u>  ACTION DUE <u>Optional Act 19. Apr</u> DUE DATE <u>3-2-02</u> INITIALS <u>J.M.</u>
2.	<input type="checkbox"/>	The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.	
3.	<input type="checkbox"/>	With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: <div style="margin-left: 20px;"> <input type="checkbox"/> the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  <input type="checkbox"/> no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.                 </div>	
4.	Further action(s):	The applicant is reminded of the following: <p>Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.</p> <p>Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).</p> <p>Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.</p>	

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231
Facsimile No. (703) 305-3230

Authorized officer S. DEVI, Ph.D.
Telephone No. (703) 308-0196

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: KRISTINA BIECKER-BRADY  
CLARK & ELBING LLP  
176 FEDERAL STREET  
BOSTON MA 02110-2214

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 00742/060W02	Date of Mailing (day/month/year) <b>02 JAN 2002</b>
International application No. PCT/US01/14372	International filing date (day/month/year) 04 MAY 2001
Applicant PRESIDENT AND FELLOWS OF HARVARD COLLEGE	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.  
**Filing of amendments and statement under Article 19:**  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):  

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
 

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. **Further action(s):** The applicant is reminded of the following:
 

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 *bis* 1 and 90 *bis* 3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer S. DEVI, Ph.D.
Facsimile No. (703) 305-3230	Telephone No. (703) 305-0196

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 00742/060W02	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US01/14372	International filing date (day/month/year) 04 MAY 2001	(Earliest) Priority Date (day/month/year) 04 MAY 2000
Applicant PRESIDENT AND FELLOWS OF HARVARD COLLEGE		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2. ☐ Certain claims were found unsearchable (See Box I).
3. ☒ Unity of invention is lacking (See Box II).
4. With regard to the **title**,
- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:
5. With regard to the **abstract**,
- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_
- ☐ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- ☒ None of the figures.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/14372

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-7 and 11-19

Remark on Protest

☐

The additional search fees were accompanied by the applicant's protest.

☐

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/14872

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 1/00, A61K 38/00; A61K 39/02, 39/08, 39/00

US CL : 530/350, 300, 825; 424/236.1, 246.1, 234.1, 184.1, 190.1

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350, 300, 825; 424/236.1, 246.1, 234.1, 184.1, 190.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DIALOG, MEDLINE, EMBASE, WEST, BIOSIS, SEQUENCE DATABASES

B moiety, anthrax toxin, muta<sup>2</sup>, pore-forming, SEQ ID NO: 12 & 21, inventors' names

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	MILLER et al. Anthrax protective antigen: Prepore-to-pore conversion. Biochemistry, 1999, Vol. 38, No. 32, pages 10432-10441, see entire document.	11-17 & 19 ----- 1-7 & 18
X --- Y	PETOSA et al. Crystal structure of the anthrax toxin protective antigen. Nature, 27 February 1997, Vol. 385, No. 6619, pages 833-838, see entire document.	1-3, 5-7, 11-17 and 19 ----- 4 and 18
X --- Y	WO 94/18332 A2 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA), 18 August 1994, see entire document.	1-3, 5-7, 11-17 & 19 ----- 4 and 18



Further documents are listed in the continuation of Box C.



See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"G"

document member of the same patent family

Date of the actual completion of the international search

26 SEPTEMBER 2001

Date of mailing of the international search report

02 JAN 2002

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

S. DEVI, Ph.D.

Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/14372

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y	US 5,677,274 A (LEPPLA et al.) 14 October 1997, see entire document.	1-3, 5-7, 11-17 & 19 ----- 4 and 18



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/14372

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-7 and 11-19, drawn to a B moiety of a pore-forming binary A-B toxin comprising a mutation, which moiety inhibits its pore-forming ability.

Group II, claim(s) 8-10 and 20-25, drawn to a method of treating or preventing bacterial infection by administering to a mammal a B moiety of a pore-forming binary A-B toxin having a mutation that inhibits its pore-forming ability or a fragment thereof.

Group III, claim(s) 26 and 27, drawn to an antibody that binds a naturally-occurring B moiety of a pore-forming binary A-B toxin.

The inventions listed as Groups I through V do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The mutant B moiety of a pore-forming binary A-B toxin or a fragment thereof is the unifying feature of the instant invention. However, such a mutant is already disclosed in the prior art. For instance, Leppla et al. (WO 94/18332) or Miller et al. (*Biochemistry* 38: 10432-10441, 1999) disclose such a mutant and therefore, the special technical feature does not define a contribution over the prior art. Invention III is directed to an antibody and does not share the same or corresponding special technical feature. It is further noted that, technically, the absence of a special technical feature would permit the separation of the method of using the product from the product itself.